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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/485,298	02/08/2000	JUNKO YAMAMOTO	1422-411P	1749

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EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/485,298	YAMAMOTO ET AL.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20,21,23,24,26-28,30,31,34,37 and 40-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20,21,23,24,26-28,30,31,34,37 and 40-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is responsive to the Amendment received on January 21, 2005.

Preliminary Remark

The addition of claims 44-48 is acknowledged.

Claim Objections

The objection of claims 42 and 43 for being dependent on subsequent claims, made in the Office Action mailed on August 20, 2004 is withdrawn as the objection contained a typographical error. The same objection should have been and is applied to claims 40 and 42, therefore.

Claim Rejections - 35 USC § 102

The rejection of claims 20 and 21 under 35 U.S.C. 102(b) as being anticipated by Auer et al. (Nucleic Acids Research, 1996, vol. 24, no. 24, pages 5021-5025), made in the Office Action mailed on August 20, 2004 is withdrawn in view of the arguments presented in the Amendment received on January 21, 2005.

Rejection – New Grounds

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 31 and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Tibbets et al. (U.S. Patent No. 5,365,455, issued November 15, 1994).

Tibbets et al. disclose a kit comprising 7-Deaza-dGTP and 7-Deaza-dATP (column 7, lines 30-40).

Therefore, Tibbets et al. anticipate the invention as claimed.

Claim Rejections - 35 USC § 103

The rejection of claims 23, 24, 26, 27, 28, 30, 34, 37, 40-43 under 35 U.S.C. 103(a) as being unpatentable over Auer et al. (Nucleic Acids Research, 1996, vol. 24, no. 24, pages 5021-5025) in view of Dodge et al. (U.S. Patent No. 5,912,117, issued June 15, 1999, 102(e) date, October 9, 1992) in light of Swanson, made in the Office Action mailed on August 20, 2004 is withdrawn in view of the arguments presented in the Amendment received on January 21, 2005.

The rejection of claim 31 under 35 U.S.C. 103(a) as being unpatentable over Auer et al. (Nucleic Acids Research, 1996, vol. 24, no. 24, pages 5021-5025), made in the Office Action mailed on August 20, 2005 is withdrawn in view of the Amendment received on January 21, 2005.

Rejection – New Grounds

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 20, 21, 31, 40, 42, 44, and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bunn et al. (U.S. Patent No. 5,213,961, issued May 25, 1993) in view of Kaiser et al. (U.S. Patent No. 5,843,669, issued December 1, 1998, filed November 29, 1996).

Claims 20, 21, 31, 40, 42, 44, and 47 are drawn to a method and kit for conducting RT-PCR, wherein during the reverse transcription step, at least one of 7-Deaza-dGTP and dITP is employed; and wherein in during the subsequent PCR (or amplification) step, at least one of 7-Deaza-dATP and dUTP is employed.

Bunn et al. disclose a method of RT-PCR, wherein the method involves the step of reverse transcribing an mRNA template into a cDNA, followed by the amplification (via PCR) of the cDNA (column 7, lines 19-28).

Bunn et al., in the process of RT-PCR do not employ the claimed nucleotide analogs in their steps.

Kaiser et al. disclose a method of amplifying (via PCR) employing 7-Deaza-dATP and 7-Deaza-dGTP) (column 24, lines 29-26; column 183, lines 1-9).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Bunn et al. and Kaiser et al. to arrive at the claimed invention for the following reasons.

The technique of RT-PCR is a well-known process of amplifying a sample in a species, wherein the target nucleic acid to be amplified is an RNA or mRNA, as evidenced by Bunn et al.

While Bunn et al., in their process of reverse-transcriptase mediated synthesis of cDNA and their subsequent amplification, involves dNTP and not their analogs as claimed, one of ordinary skill in the art at the time the invention was made would have been motivated to employ the dNTP nucleotide analogs of Kaiser et al. for the advantage provided their use, the advantage of which had been explicitly disclosed by Kaiser et al.:

"The 7-deaza purine analogs (7-deaza-dATP and 7-deaza-dGTP) serve to ***destabilize regions of secondary structure by weakening the intrastrand stacking of multiple adjacent purines. This effect can allow amplification of nucleic acids that, with the use of natural dNTPs, are resistant to amplification because of strong secondary structure***" (column 183, lines 1-8).

Hence, one of ordinary skill in the art at the time the invention was made would have been motivated to improve the amplification reaction of Bunn et al., whether it be reverse transcription reaction or the subsequent amplification reaction, with the 7-deza nucleotide analogs of Kaiser et al, because by doing so, one of ordinary skill in the art would have been able to amplify target nucleic acids having a strong secondary structure.

One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success at such combination as the incorporation of nucleotide analogs during primer extension as already been demonstrated to be feasible by Kaiser et al.

With regard to the kit comprising the elements, it would further have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to package the reagent compositions of Bunn et al. and Kaiser et al. into kits in view of the conventionality of kits in the analytical arts for the advantages of convenience, cost-effectiveness, matched and/or preweighed components, etc.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Claims 23, 24, 26, 27, 28, 30, 34, 37, 43, 45, 46, and 48 rejected under 35 U.S.C. 103(a) as being unpatentable over Bunn et al. (U.S. Patent No. 5,213,961, issued May 25, 1993) in view

of Kaiser et al. (U.S. Patent No. 5,843,669, issued December 1, 1998, filed November 29, 1996) and in light of Fuller (U.S. Patent No. 5,432,065, issued July 11, 1995).

Bunn et al. disclose a method of RT-PCR, wherein the method involves the step of reverse transcribing an mRNA template into a cDNA, followed by the amplification (via PCR) of the cDNA (column 7, lines 19-28).

Bunn et al., in the process of RT-PCR do not employ the claimed nucleotide analogs in their steps.

Bunn et al. do not explicitly teach a method and a kit for employing a compound that lowers Tm (melting temperature) value of a double-stranded nucleic acid, wherein said compound is selected from the group consisting of formamide, dimethyl sulfoxide, and trimethyl glycine.

Kaiser et al. disclose a method of amplifying (via PCR) employing 7-Deaza-dATP and 7-Deaza-dGTP) (column 24, lines 29-26; column 183, lines 1-9).

Fuller discloses a method of amplifying a nucleic acid (column 1, line 46), wherein said method involves the use of 7-deaza nucleotide, specifically 7-deaza-dGTP (column 7, line 15), in a solution containing formamide (column 7, lines 20-21).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Bunn et al. and Kaiser et al. and Fuller et al. to arrive at the claimed invention for the following reasons.

The technique of RT-PCR is a well-known process of amplifying a sample in a species, wherein the target nucleic acid to be amplified is an RNA or mRNA, as evidenced by Bunn et al.

While Bunn et al., in their process of reverse-transcriptase mediated synthesis of cDNA and their subsequent amplification, involves dNTP and not their analogs as claimed, one of ordinary skill in the art at the time the invention was made would have been motivated to employ the dNTP nucleotide analogs of Kaiser et al. for the advantage provided their use, the advantage of which had been explicitly disclosed by Kaiser et al.:

"The 7-deaza purine analogs (7-deaza-dATP and 7-deaza-dGTP) serve to ***destabilize regions of secondary structure by weakening the intrastrand stacking of multiple adjacent purines. This effect can allow amplification of nucleic acids that, with the use of natural dNTPs, are resistant to amplification because of strong secondary structure***" (column 183, lines 1-8).

Hence, one of ordinary skill in the art at the time the invention was made would have been motivated to improve the amplification reaction of Bunn et al., whether it be reverse transcription reaction or the subsequent amplification reaction, with the 7-deza nucleotide analogs of Kaiser et al, because by doing so, one of ordinary skill in the art would have been able to amplify target nucleic acids having a strong secondary structure.

One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success at such combination as the incorporation of nucleotide analogs during primer extension as already been demonstrated to be feasible by Kaiser et al.

With regard to the inclusion of a compound that lowers the melting temperature of a double-stranded nucleic acids, wherein said compound is a formamide, such inclusion would have also been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made based on the explicit teaching of Fuller:

"This invention provides an alternative to these procedures, and involves use of a denaturing reagents which decreases the melting temperature of the DNA. Some DNA denaturing reagents e.g., urea and formamide, do decrease the melting temperature of DNA by about 0.5°C for each 1% (vol/vol) concentration" (column 3, lines 3-5, Fuller).

It is well known that for an amplification reaction to occur, the amplification primers must hybridize to single-stranded nucleic acid templates. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to combine the reagents that preclude template double-strand formation, via use of 7-deaza nucleotide analogs as well as formamide.

As Fuller demonstrates that amplification with solution containing formamide and at least one 7-deaza nucleotide analog (specifically, 7-deaza-dGTP) has been feasible, one of ordinary skill in the art would have had no doubt that addition of an additional 7-deaza nucleotide analog as that of Kaiser et al. would have worked equally well, giving said ordinarily skilled artisan a reasonable expectation of success at such combination.

With regard to the kit comprising the elements, it would further have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to package the reagent compositions of Bunn et al., Kaiser et al., and Fuller into kits in view of the conventionality of kits in the analytical arts for the advantages of convenience, cost-effectiveness, matched and/or preweighed components, etc.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Claim 41 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bunn et al. (U.S. Patent No. 5,213,961, issued May 25, 1993) in view of Kaiser et al. (U.S. Patent No. 5,843,669, issued December 1, 1998, filed November 29, 1996) and Keller (U.S. Patent No. 5,356,796, issued October 18, 1994).

The teachings of Bunn et al., and Kaiser et al., have already been discussed above.

The artisans do not explicitly disclose a kit comprising a compound for lowering Tm value of a double-stranded nucleic acid and a thermostable DNA polymerase.

Keller discloses a method of conducing PCR in a solution, wherein the method employs reagents, 3% formamide, 5μl Taq buffer, and 2 units Taq polymerase, which is known in the art for being thermostable (column 26, lines 59-66).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Bunn et al., Kaiser et al., and Keller to arrive at the claimed invention for the following reasons.

The method conducted by Bunn et al. and Kasier et al. involves first the reverse transcription of an RNA or mRNA into a cDNA, followed by the amplification of the cDNA.

Further, it is well-known in the art that for an amplification reaction to occur, the amplification primers must hybridize to single-stranded nucleic acid templates. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to combine a compound that precludes template double-strand formation, such as that of Keller in the amplification reaction of Bunn et al., and Kaiser et al. with a reasonable expectation of success.

As the method produced by the combination of the artisans is determined to be obvious, it would further have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to package the reagent compositions of Bunn et al., Kaiser et al., and Keller into a kit in view of the conventionality of kits in the analytical arts for the advantages of convenience, cost-effectiveness, matched and/or preweighed components, etc.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Conclusion

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m. The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Primary Examiner in charge of the prosecution, Dr. Kenneth Horlick, can be reached at (571) 272-0784. If the attempts to reach the above Examiners are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a

general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Young J. Kim
Patent Examiner
Art Unit 1637
4/18/05

YOUNG J. KIM
PATENT EXAMINER

yjk